## REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application are respectfully requested in light of the amendments above and the comments that follow. By this amendment, claims 16 and 31 are amended. Support for the claim amendments is found in the previously presented claims, and in the Examples. Upon entry of the present Response, Claims 16 – 17, 19 – 32 are pending and await further consideration on the merits.

## CLAIM REJECTIONS UNDER OBVIOUSNESS-TYPE DOUBLE PATENTING

Examiner provisionally rejected Claims 16, 17 and 19–31 on the grounds of nonstatutory obviousness-type double patenting over Claims 1 – 13 of U.S. Application No. 10/522,234 ("the '234 application") and Claims 16, 17 and 19 – 31 of U.S. Application No. 11/583,940 ("the '940 application").

Applicants note that the '234 application is abandoned. As such, Applicants respectfully request this rejection be withdrawn.

Examiner alleges that the instant claims are rendered obvious over the claims of '940 application because the '940 has a solubilizing agent. Applicants respectfully disagree. The instant claims and invention are to a core comprising at least one active principle and at least one solubilizing agent where the at least one solubilizing agent is capable of increasing the solubility of the at least one active principle by more than 50% when the at least one solubilizing agent is placed in an aqueous solution at a concentration of 20% w/w at 37°C. The '940 application, however, does not disclose use of at least one solubilizing agent in a core. Further, the '940 application does not teach nor suggest use of at least one solubilizing agent in a core. Moreover, the '940 application does not disclose that the compositions disclosed can be adjusted such that the solubility of the active principle increases by more than 50% when the at least one solubilizing agent is placed in an aqueous solution at a concentration of 20% w/w at 37°C.

As such, the instant claims are neither anticipated nor rendered obvious by this reference. Applicants therefore request the rejection be withdrawn.

**REJECTIONS UNDER 35 U.S.C. § 102**

Claims 16, 17, 19-26 and 28-31 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mehta (U.S. Patent 5,084,278). Applicants respectfully traverse this rejection for the reasons detailed below.

To find anticipation under 35 U.S.C. § 102, every element of the claims must be taught in a single reference. *See, e.g., Carella v. Starlight Archery and Pro Line Co.* , 804 F.2d 135, 138 (Fed. Cir. 1986).

Specifically, the Examiner alleges that Mehta anticipates the instant claims because it discloses a core comprising an active agent and diluent (which the Examiner— without any evidence— alleges is a solubilizing agent), coated with a film forming polymer. The polymers may include at least 5% of high temperature and 5% of a low temperature polymer, and a lubricant. Office Action at pages 3 – 4.

Examiner's unsupported suggestion that the diluent of Mehta is in fact a solubilizing agent ignores the clear teaching of the reference as well as the claims. As indicated by the title, Mehta teaches "Taste-Masked Pharmaceutical Compositions." As indicated in the Background, the invention of Mehta "relates to novel taste-masked pharmaceuticals and to taste-masked pharmaceuticals capable of being chewed without producing a taste." Col. 1, ll. 5 – 7. Similarly, the Summary of the invention clarifies that the invention is directed to blocking the taste of the medicament (See Col. 3) and ensuring that the medicament is not released in the "limited amount of fluid that exists in the mouth during chewing."

In both the text and the claims, Mehta uses functional language to make it clear that the invention is chewable and taste masking. *See, e.g.*, Claim 1. Given this express teaching of Mehta to mask taste and not be released- even in the mouth when chewing- it is unreasonable for

the Examiner to take the position that the dry diluents of Mehta, which are used to reduce the concentration of the dry active ingredient in the Mehta compositions, are really used for solubilizing the ingredients. Such solubilization would make it more difficult to block the taste, which is the entire purpose of the Mehta teaching. Given the fact that solubilization runs counter to Mehta, Applicants again request the Examiner provide evidence that the diluents of Mehta are - in reality - simply solubilizers.

Moreover, Mehta does not teach all elements of the instant claims. Claim 16 is to:

> Orally administered microcapsules for modified release of at least one active principle with low solubility,
> wherein the mean diameter of the microcapsules are less than 1000 microns;
> wherein each microcapsule has a core comprising at least one active principle and at least one solubilizing agent,
> wherein the at least one solubilizing agent increases the solubility of the at least one active principle by more than 50% when the at least one solubilizing agent is placed in an aqueous solution at a concentration of 20% w/w at 37°C;
> wherein the at least one solubilizing agent confers properties upon the core such that in a dissolving test (TD) a non-coated core releases 80% of the at least one active principle in less than two hours;
> wherein the core is coated with a coating film which controls the modified release of the active principles;
> wherein the coating film is between at least about 3% and about 7% dry weight/dry weight of the microcapsule mass;
> wherein the coating film of each microcapsule comprises at least one film-forming polymer (P1) insoluble in gastrointestinal tract fluids, at least one water-soluble polymer (P2),and at least one plasticizer, (PL).

Thus, the instant claim requires the coating film be between about 3% and about 7% dry weight/dry weight of the microcapsule mass.

Mehta, however, teaches that the coating is 20 – 40% by weight of the microcapsules. See, Col 10, ll. 30 – 21, 63 – 65. This teaching of Mehta is expected for the use that Mehta teaches: blocking taste. Mehta is directed to compositions that mask taste so the drug, when chewed, does not produce a bitter taste. *See*, Mehta at Col. 1, ll. 6 – 8. The purpose of making

such a composition is to increase patient compliance, especially for children who may chew the pharmaceutical. *Id.* at Col. 1, ll. 32 – 46.

In contrast, the instant invention solves an entirely different problem- controlling low solubility active principle release. See, ¶ 1 – 2. As noted in ¶¶ 12 – 17, control of the coating thickness and composition for an active principle of low solubility is difficult. If the coating is too thin, the film may not be even or difficult to reproduce. If the coating is too thick, the active principle drug release is slow or nonexistent. Applicants are credited with finding that the range of between about 3% and about 7% dry weight/dry weight of the microcapsule along with other claim limitations produces the desired effect. Mehta not only does not teach this range of coating, but instead teaches the substantially higher range of 20 – 40% by weight of the microcapsules and teaches away from the composition of the invention. Similarly, Mehta would not be concerned with hiding the taste of low solubility medicaments: they would not solubilize and would not lead to a bitter taste. *Id.*, Col. 1, l. 8.

A reference such as Mehta that teaches taste masking is fundamentally inconsistent with a product that increases solubility. The increase in solubility would make it more likely that the substance would reach and interact with the taste receptors of the tongue. Thus, the fact that the different compositional limitation in Mehta may overlap with the compositional limitations of certain claims of the instant application is irrelevant to the claimed composition, which includes the solubility of greater than 50% in an aqueous solution of 20% w/w at 37°C. To argue otherwise ignores the functional language of Mehta's and Applicants' claims.

In addition, the higher range of coating for Mehta is logical and expected, because it is more likely that a thicker coating (20 – 40%) would mask taste as opposed to a thinner coating. For Mehta, coatings are used to provide a diffusion barrier. According to Fick's first law of diffusion, the diffusion flux (or rate of transfer) is inversely proportional to the distance x (thickness).

$$J = -D\frac{\partial \phi}{\partial x}$$

Thus, a thicker coat would decrease diffusion flux, and less bitter-tasking drug is released. For this reason, to reach a goal of taste masking one of skill in the art would of course think to apply a thicker coat, not a thinner coat. As such, Applicants respectfully request the rejection be withdrawn.

In addition to the teaching away from the functional limitations, Mehta does not teach or suggest all of the claimed ranges of the composition. The claims are limited to the mass fraction by dry weight of film-forming polymer (P1) relative to the total mass of the coating is between 40 and 90% and the mass fraction by dry weight of the water-soluble polymer (P2) P2/P1+P2 is between 15 and 60% relative to the total mass of the coating.

In contrast Mehta merely teaches "at least about 5%." *See*, Mehta at Col. 4, ll. 23 – 28.

A genus can only anticipate a species if one of ordinary skill in the art is able to "at once envisage" the species compound within the chemical formula of the genus compound. *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962); see also *In re Meyer*, 599 F.2d 1026, 202 USPQ 175 (CCPA 1979) (A reference disclosing "alkaline chlorine or bromine solution" embraces a large number of species and cannot be said to anticipate claims to "alkali metal hypochlorite."). Thus, the Examiner must show that one or ordinary skill in the art would be able to "at once envisage" the species ranges.

There is no evidence, however, that one viewing Mehta's "at least about 5%" would envisage the species. The instant invention is to enhance and control release of a low solubility active principle whereas Mehta is to a different area of the pharmaceutical arts: that of masking taste by limiting the release of a highly soluble active principle with a disagreeable taste. There is no evidence that one of skill in the art would apply the teaching of Mehta to any field except taste masking, certainly not an art that would enhance solubility and make it more likely the active ingredient would reach the taste buds and not mask the taste. Further, there is no evidence that one of ordinary skill in the art would take the very liberal genus of "at least about 5%" and immediately envisage the specific species of P1 being between 40 and 90% and P2 being between 15 and 60% relative to the total mass of the coating.

In addition, Applicants submit that the Examiner is picking and choosing from different portions of Mehta and adding the Examiner's own hindsight, which does not constitute anticipation, nor does it in any way demonstrate each element of the instant claims. Further, Applicants note that for a reference to anticipate, the "elements must be arranged as required by the claim." *See*, MPEP 2131 (citing *In re Bond*, 910 F.2d 831 (Fed. Cir. 1990)). Mehta, however, does not even teach the elements arranged as required by the claim.

Even if the claimed subject matter could be divined from Mehta, it is well established that picking and choosing from different portions of a reference does not constitute anticipation. *See, In re Arkley,* 455 F.2d 586, 587 (CCPA 1972) (reversing the Examiner's 35 U.S.C. §102 rejection because the single Flynn reference did not clearly and unequivocally disclose the invention "without any need for picking, choosing, and combining" various portions of the reference that were directly related to each other); *see also, In re Wiggins*, 488 F.2d 538, 543 (CCPA 1973) (reversing the Examiner's 35 U.S.C. §102 rejection because the compounds, though named in the asserted reference, were not actually prepared). Instantly, the Office has given no rationale for the "picking and choosing" of portions of the Mehta reference, or how the portions would logically be assembled to anticipate the instant claims.

The instant specification also explains how to use the composition to form compounds with the desired properties: properties completely counter to those taught by Mehta. Mehta, in contrast to the Applicant's invention, has a laundry list of seven paragraphs of compounds that may be "high temperature film forming polymers." *See*, Mehta from Col. 4, l. 24 – Col. 5, l. 55. Applicants submit that although these compounds are named in the reference, there is no evidence that the compounds were actually prepared and have the properties of the instantly claimed dosage forms. Indeed, as explained *supra*, it is more likely that they would have difficulty in satisfying the functional requirements of Mehta. The picking and choosing from the laundry list of compounds by the Examiner does not constitute anticipation, especially when making the composition less soluble and able to mask taste was the intended purpose.

In addition, Applicants submit that Mehta cannot anticipate the current claims because Mehta is so vague and obtuse that it is unclear which compounds are "high" or "low" temperature film forming polymers and how they are to be combined and/or used. For example, Mehta states an example of a high temperature film-forming polymer is Eudragit E100. *See*, Mehta at col. 5, l. 18. Mehta then states an example of a low temperature film-forming polymer is Eudragit E100. *See*, Mehta at col.6, l. 6. Thus, according to Mehta, one compound can be both a high temperature and low temperature film-forming polymer. This lack of clear delineations between the polymers of Mehta, combined with picking and choosing by the Examiner, further combined with Examiner's hindsight, would thus still not result in the elements of the claims arranged as required by the claims.

As Claims 17, 19 – 26 and 28 – 31 contain the limitations from independent Claim 16, Mehta cannot anticipate the dependent claims. For at least these reasons, Applicants respectfully request the rejection of Claims 16, 17, 19-26 and 28-31 under 35 U.S.C. § 102(b) be withdrawn.

**REJECTION UNDER 35 U.S.C. § 103**

Claims 16 – 17 and 19 – 31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mehta (U.S. 5,084,278), in view of Mulye (U.S. 6,946,146).

The Office appears to apply the rejection under a Teaching, Suggestion and Motivation analysis. The Applicants traverse the rejection as such. Under such analysis, to establish a *prima facie* case of obviousness under this analysis, three basic criteria must be met. First, the prior art reference must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Finally, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986). As explained above, Mehta neither teaches the claimed invention nor

would be modified to teach the claimed invention. Blocking solubilization to mask taste without an overcoat, as in Mehta, is fundamentally different from limiting the overcoat to increase solubilization, as in the claimed invention. Indeed, the Examiner's suggestion that using a surfactant would be combined with an attempt to limit solubilization to hide the taste of the drug is unreasonable since a surfactant would be expected to increase many forms of solubilization and would make masking the taste more difficult as it decreased surface tension of the dissolving liquid.

The Office fails to establish a ***prima facie*** case of obviousness under the analysis. For instance, there is no suggestion or motivation to modify the reference or to combine reference teachings. Mehta teaches coatings to mask taste, whereas Mulye teaches latex dispersion coats to control release of a drug. Mehta teaches microcapsules of 0.25 – 1mm in diameter, and Mulye doesn't teach a microcapsule of any diameter. Indeed, Mehta and Mulye are so distinct that the Examiner only relies on Mulye to teach use of a surfactant. Office Action at pages 8 – 9. There is no suggestion or motivation to modify or combine these references. In addition, there must be a reasonable expectation of success. As the Examiner concedes, Mehta does not teach use of a lubricant such as the stearate.

Second, Examiner has not shown a teaching or suggestion to make the claimed invention, with any reasonable expectation of success. These elements must be found in the prior art. *In re Vaeck*, 947 F.2d 488; *Hodosh*, 786 F.2d 1143 n.5. The Examiner has not shown where in the art the addition of a lubricant, which is known to alter the chemical properties, to Mehta would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Further, even if there was a teaching or suggestion to make the claimed invention, Applicant submits that one of skill in the art would not have a reasonable expectation of success because Mehta is so vague and obtuse. As stated above, Mehta is unclear which compounds are "high" or "low" temperature film forming polymers and how they are to be combined and/or used. For example, Mehta uses Eudragit E100 as an example of both a high and low temperature film-forming polymer is. *See*, Mehta at col. 5, l. 18, col.6, l. 6. Thus, according to Mehta, one

compound can be both a high temperature and low temperature film-forming polymer. One with skill in the art would not have a reasonable expectation of success, because they would not know how to combine the vague and confusing Mehta with Mulye.

For at least these reasons, the Applicants believe the Office has failed to meet their burden under Teaching, Suggestion and Motivation analysis and requests the rejection be withdrawn.

Even if Examiner rejected the claims under another analysis, the Applicants still believe the rejection is in error because one of skill in the art would find these references are nonanalogous art. To determine if two references are analogous, the court has found "the similarities and differences in structure and function of the inventions to carry far greater weight." *In re Ellis*, 476 F.2d 1370, 1372, 177 USPQ 526, 527 (CCPA 1973). Further, references which do not teach the same or similar problems are not analogous. See, MPEP 2141.01(a) citing *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983). (To determine if analogous, court examined references to find if the references had the same and similar problems.).

Mehta and Mulye are nonanalogous arts because their coatings have a different structure composition to serve different purposes. Their problems are in no way same or similar.

Mulye, for example, uses a latex dispersion containing a polymer insoluble in acidic, basic and neutral pH. The problem that Mulye tries to solve is to control release of a drug by using a coating that gives low, continuous drug release. *See*, Mulye at Figure 1 – 3, abstract. Mulye goes through at great length to describe how others in the prior art attempt to use a rate controlling membrane surrounding a core to control drug release. See, *Id.* at Col. 1 – 4. Further, Mulye explains that his invention "relates to a controlled release formulation of a therapeutic agent and in particular, to a sustained release formulation in which a solid substrate containing the active ingredient is provided with a coating which regulates the release of the active ingredient." *Id.* at Col. 1 "Field of the Invention." Further, Mulye describes sustained and controlled release to mean the release of the drug as to maintain blood levels within the

therapeutic range over an extended period of time, e.g., 4 to 24 hours or even longer. *Id.* at Col. 5, ll. 18 – 24.

In contrast, Mehta uses high and low temperature polymers to form a coating over a drug. The problem that Mehta is trying to solve is to use a coat to hide taste. Generally, Mehta is directed to a composition that masks taste so the drug, if chewed, does not produce a bitter taste. *See*, Mehta at Col. 1, ll. 6 – 8. The purpose of making such a composition is to increase patient compliance, especially for children who may chew the pharmaceutical. *Id.* at Col. 1, ll. 32 – 46.

The purpose of taste making and the controlling drug release profiles are dissimilar. In addition, the reference did not have the same or similar problems. One reference had a problem of drug compliance based on drug taste, and the other reference had the problem of maintaining blood levels with a therapeutic range for an extended period of time.

As such, one of skill in the art would not look to combine Mulye (coating to maintain blood levels) with Mehta (coating to mask taste) to cure one or more deficiencies with Mehta. The references do not teach the same or similar problem and have a different purpose. Thus, the references are nonanalogous art.

For this same reason, one of skill in the art would not look to use Mulye to cure any deficiencies for Mehta. As such, the obviousness rejection is in err, and Applicants request the rejection be withdrawn.

In addition, the Examiner alleges that Mehta and Mulye teach identical chemical structures, and thus the properties disclosed/claimed by Applicants are necessarily present. *See*, Office Action at 4. Applicants disagree.

Constituents, such as polymers, that belong to the same chemical group can have very different products and piece. These properties are well known and a matter of common knowledge to one of skill in the art. For example, all of the Mulye applications below use starch (CAS Registry No. 9005-25-8) for very different reasons.

- Mulye teaches a seed may be a starch sphere of from about 0.5 mmm to about 1.5 mm. *See* Mulye, Col. 10, ll. 52 – 54.
- Mulye teaches binder may be pregelatinized starch. *Id.* at Col. 10, l. 64 – Col. 11, l. 3.
- Mulye teaches a swellable polymer may include a starch. *Id.* at Col. 11, l. 29.

Still others use starch in oral preparations to change the following: flow properties, viscosity, adhesiveness, shelf-life stability, anti-caking, hygroscopicity, freeze-thaw stability, opacity, oil retention, mouthfeel, crystallinity, color, swelling property, and as a dispersing agent. Indeed, the physical properties of starch vary widely and are dependent upon the source, and amylose and amylypectin content. For instance, starch made from Waxy Rice has 0% amylose, starch from corn has 28% starch, and starch from potato has 20% amylose. For this reason, although starch is the ingredient in various foods like noodles, mashed potatoes, breads, pancakes, blintzes, cereals, pasta, chapatis, flour tortillas, etc., these preparations that do not share the same physical properties. Thus, when devising a new formulation, the grade, process, and in particular the quantities and the physical treatments of the various compounds used will result in a formulation that have very little physical characteristics in common with formulations of the prior art using the "same" (from a chemical standpoint) starting ingredients. For at least this reason, Applicant asserts that Mehta and Mulye do not teach the "identical chemical strucutre" of the instant claims; this is clear through the use of the functional language and descriptive content of their disclosures.

Applicants respectfully traverse this rejection as Mulye does not cure the deficiencies of Mehta. As Claims 16 – 17 and 19 – 31 contain the limitations from independent Claim 16, Applicants respectfully request that the rejection to Claims 16 – 17 and 19 – 31 under 35 U.S.C. § 103(a) be withdrawn.

## CONCLUSION

In view of the above remarks and amendments, the Applicants respectfully submit that each of the pending objections and rejections has been addressed and overcome, placing the present application in condition for allowance. A notice to that effect is respectfully requested.

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact the undersigned. Should there be any outstanding matters that need to be resolved in the present application; the Examiner is respectfully requested to contact the telephone number of the undersigned below.

Applicants submit concurrently a request for a three-month extension of time under 37 C.F.R. § 1.136 and the accompanying fee. Applicant also submits concurrently a Request for Continued Examination pursuant to 37 C.F.R. § 1.114. Please charge our Credit Card in the amount of $1,920.00 covering the fees set forth in 37 C.F.R. § 1.17(e) and 1.17(a)(3). In the event that any additional extensions of time are necessary to prevent the abandonment of this patent application, then such extensions of time are petitioned. The U.S. Patent and Trademark Office is authorized to charge any additional fees that may be required in conjunction with this submission to Deposit Account Number 50-2228, under Order No. 022290.0123PTUS from which the undersigned is authorized to draw.

Dated: February 19, 2009

Respectfully submitted,

By_____

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